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LETTERS TO THE EDITOR

Dedicated to V. F. Mironov on His 60th Anniversary

Synthesis of *p-tert*-Butylthiacalix[4]arene with Spatially Separated Phosphoryl and Amino Groups

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Abstract—The reactions of *p-tert*-butylthiacalix[4]arenes containing phthalimide fragments with diethyl-[(*p*-toluenesulfonyl)oxymethyl)]phosphonate were used to synthesize new phosphonate derivatives in the *1,3-alternate* configuration. Hydrolysis and hydrazinolysis of the products gave the corresponding amido- and aminophosphonate thiacalixarene derivatives. ^{1}H–^{1}H NOESY NMR spectroscopy established a *1,3-alternate* configuration of the synthesized macrocycles with spatially separated phosphoryl and amino groups.

Keywords: thiacalix[4]arene, phosphorylation, phosphonates, macrocycles

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Thiacalixarenes have been successfully used for a few decades in one of advanced fields of supramolecular chemistry, specifically, design of synthetic receptors capable of recognizing and binding various molecular objects [1–6]. These macrocyclic condensation products of *p*-substituted phenols and sulfur present a synthetic platform which can be easily modifies in both the upper and lower rims. This feature, as well as the fact that these macrocycles can exist in several spatial configurations (*cone*, *partial cone*, and *1,2-* and *1,3-alternates*) make it possible to fix a definite spatial arrangement of different (poly)-functional fragments capable of specifically reacting with substrates [7–10].

Such polyfunctional compounds as aminophosphonates attract attention due to their versatile properties. They are strong complexing agents, inhibitors of metabolic processes, and show herbicide, antibacterial, and antiviral properties [11–15].

The receptor affinity of aminophosphonates to specific substrates is determined by their phosphoryl and amine functions. The thiacalixarene platform allows spatial separation of these two functional groups, and this may result in new structures with interesting properties. Thus, the goal of the present work was to synthesize thiacalix[4]arenes with separated phosphoryl and amino groups.

First, using published procedures, we synthesized the starting compounds, specifically, mono- (**1**) [16] and diphthalimide (**2**) [17] derivatives of *p-tert*-butylthiacalix[4]arene. Further on compounds **1** and **2** were reacted with diethyl[(*p*-toluenesulfonyl)oxymethyl]phosphonate [18] to obtain phosphonate derivatives of thiacalixarene **3** and **4** (Scheme 1). The optimal solvent for the reaction is THF and the optimal base is cesium carbonate. With weaker bases (potassium and sodium carbonates), hardly separable product mixtures were obtained.

Alkaline hydrolysis of diphosphonate **4** in aqueous THF resulted in a partial opening of the phthalimide group to form amidoacid **5** and did not involve the ethoxy groups on phosphorus (Scheme 2). On the other hand, hydrazinolysis of compound **4** removed the protective phthalimide groups and gave the target compound **6**.

The composition and structure of compounds **3–6** were confirmed by elemental analysis and physicochemical methods (IR and ^{1}H, ^{31}P, and ^{13}C NMR spectroscopy and mass spectrometry). Two-dimensional ^{1}H–^{1}H NOESY NMR spectroscopy established that compounds **3** and **4** are exist in a *1,3-alternate* configuration.

5,11,17,23-Tetra-*tert*-butyl-25,26,27-tris[(*O*,*O*-diethylphosphoryl)methoxy]-28-(2-phthalimidoethoxy)-